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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/058,546	04/10/1998	WALTER H. GUNZBURG	GSF98-02A	7592

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EXAMINER
WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
1633	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 09/058,546	Applicant(s) GUNZBURG ET AL.	
	Examiner Michael Wilson	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2001*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-61* is/are pending in the application.

4a) Of the above claim(s) *1-12,18,24,25,29,30,33-38,44,49,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-16,19-23,26-28,31,32,39-43,45-48,50-53 and 56-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

Election/Restriction

Claims 1-4, 9-11, 33-38, 44 and 49 as newly amended and new claims 54 and 55 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims encompass retroviruses comprising RNA which is equivalent to the non-elected invention of retroviruses comprising antisense. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1-4, 9-11, 33-38, 44, 49, 54 and 55 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

This application contains claims 1-12, 18, 24, 25, 29, 30, 33-38, 44, 49, 54 and 55 drawn to an invention nonelected with traverse in Paper No. 17. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 13-16, 19-23, 26-28, 31, 32, 39-43, 45-48, 50-53 and 56-61 are under consideration in the instant office action.

Applicant's arguments filed 10-15-01 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

1. Claims 13-16, 19-23, 26-28, 31, 32, 41-42, 45-48, 50-53 and 56-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a stably transfected packaging cell line comprising a nucleic acid sequence encoding a retroviral vector encoding SDI-1 operably linked to a promoter, transducing cells *in vitro* with a retroviral particle encoding SDI-1, and a method of treating restenosis by introducing, by catheter or direct injection, into a blood vessel at a site of restenosis, a retroviral vector encoding SDI-1 operably linked to a promoter, resulting in reduction of intimal hyperplasia, does not reasonably provide enablement for fragments or analogs of SDI-1, treating any disease, treating any symptom of cancer or restenosis, using any mode of delivery, capsules comprising producer cells, methods of using such capsules, pharmaceutical compositions comprising producer cells, or methods of using such pharmaceutical compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 15, 16, 20-23, 41-42, 46, 47, 51, 52 and 56-61, encompassing capsules comprising packaging cells, pharmaceutical compositions comprising packaging cells, and methods of using such capsules or pharmaceutical compositions, are not enabled for reasons of record. The only disclosed use for the capsules and pharmaceutical compositions comprising producer cells are for therapy *in vivo*. If applicants can point to another purpose for the capsule or pharmaceutical composition, please point to such a purpose by page and line number.

Crystal (1995, Science, Vol. 270, page 404-410; page 409) and Feldman (1995, Fundamental & Clin. Pharm., Vol. 9, pages 8-16), both of record, taught the combination of vector and mode of delivery for gene therapy required to target the desired tissue and provide adequate expression of a protein such that a desired effect was obtained was unpredictable. Nabel (US Patent 5,863,904, Jan. 26, 1999) taught administering a viral vector encoding SDI-1 to a restenosis patient by catheter or direct injection into a blood vessel at the site of restenosis resulting in a decrease in the intimal hyperplasia in said blood vessel (claim 1; col. 3, line 10). The art at the time of filing did not teach how to administer retroviral packaging cells or capsules comprising retroviral packaging cells to patients such that a therapeutic effect was obtained. Therefore, it was unpredictable how to administer retroviral packaging cells or capsules comprising retroviral packaging cells to patients such that a therapeutic effect was obtained. Thus, one of skill in the art at the time the invention was made would have been limited to using retroviral particles encoding SDI-1 to treat restenosis as taught by Nabel.

Applicants argue one likely mode of administration is injection of capsules. Applicants ague is not persuasive. Applicants do not overcome the unpredictability in the art by teaching the dosage or route of administration of retroviral packaging cells or capsules comprising retroviral packaging cells required to target cells of interest *in vivo*, provide a therapeutic level of retroviral particle production *in vivo*, or provide a therapeutic effect. Applicants have not correlated administering retroviral particles encoding SDI-1 for treating restenosis as taught by Nabel to administering packaging cells or capsules such that the same tissue is targeted, equivalent

amounts of retroviral particles are contacted with the tissue or that a therapeutic effect is obtained. Because of the dearth in the art regarding how to use retroviral packaging cells or capsules comprising retroviral packaging cells to treat disease taken the with the lack of guidance in the specification, applicants have not enabled one of skill to use retroviral packaging or capsules comprising retroviral packaging cells to treat disease.

Claims 13-16, 19-23, 26-28, 31, 32, 45-48 and 50-53, encompassing retroviral particles encoding SDI-1 analogues or functional fragments of SDI-1, are not enabled for reasons of record. Applicants argue amino acids 1-71 and 42-58 of the SDI-1 protein as described by El-Deiry, Harper or Xiong are the same and have the desired function. First, the examiner cannot determine by eye that amino acids 1-71 of El-Deiry, Harper and Xiong are 100% identical. Secondly, it cannot be determined from page 9, line 5, which states amino acids 1-71 and other fragments of the 164 amino acids may have equivalent biological activity to full length SDI-1; however, the specification does not provide an assay for determining fragments of SDI-1 that have the same function as full length SDI-1. Therefore, the mere statement is not adequate to enable fragments of SDI-1. Similarly, the specification teaches amino acids 42-58 of SDI-1 may be employed; however, the specification does not teach amino acids 42-58 has equivalent biological activity as full length SDI-1.

Applicants argue the specification teaches how to determine analogues of SDI-1 on page 9, lines 13-24. Applicants argument is not persuasive. The citation provides methods of making mutations in SDI-1, but does not teach an assay to determine whether the mutants have the

desired function. Nor does the specification teach the amount of hybridization or the hybridization conditions required to determine mutants that have the same function as full length SDI-1.

2. Claims 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 32 as newly amended are indefinite. If applicants intend the claim to encompass administering retroviral particles or packaging cells producing retroviral particles, then parent claims should not be limited to administering retroviral particles. Administering retroviral particles in parent claim 27 does not encompass administering packing cells producing retroviral particles. If packaging cells are administered, retroviral particles are produced *in vivo*, they are not "administered". Clarification is required.

Claim Rejections - 35 USC § 103

3. Claims 13, 14, 19, 26-28, 31, 32, 39, 40, 45, 48, 50 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller (Miller et al., 1989, Biotechniques, Vol. 7, pages 980-990) or Price (Price et al., 1987, PNAS, USA, Vol. 84, pages 156-160) in view of Nabel (Nabel et al., US Patent 5,863,904, Jan 26, 1999).

Miller and Price taught stably transfected packaging cells producing retroviral particles (see page 981, column 1, column 3 and page 156, column 2, line 18, respectively). The packaging cells are suspended in culture media which is a "carrier" as claimed. Miller and Price did not teach the retroviral particles encoded SDI-1 or treating restenosis using retroviral particles encoding SDI-1. However, Nabel taught retroviral particles encoding SDI-1 and injecting viral particles into a patient to treat restenosis (see abstract; col. 3, line 10; col. 4, line 60; claim 1; col. 3, line 10). The SDI-1 protein of Nabel encodes full length SDI-1; therefore, the retroviral particle of Nabel encodes full length SDI-1 which comprises amino acids 1-71 and 42-58 of SDI-1 as claimed. The limitation of a pharmaceutical composition is an intended use and does not bear patentable weight in considering the art.

Thus, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to make a stably transfected packaging cell that produces retroviral particles as taught by Miller or Price to make retroviral particles encoding SDI-1 as taught by Nabel. One of ordinary skill would have been motivated to make retroviral particles encoding SDI-1 using the methods taught by Miller or Price because Miller and Price state the retroviral particles can be used *in vivo* (page 989, last sentence and page 157, column 1, fourth paragraph, respectively) and because Nabel taught making and using retroviral particles encoding SDI-1 to treat restenosis (col. 3, line 10).

Applicants argue the combined teachings of Miller or Price taken with Nabel would not result in a stably transfected packaging cell. Applicants argument is not persuasive because

Miller and Price obtained stably transfected packaging cells that produce retroviral particles. Therefore, one of ordinary skill would have had a reasonable expectation of success in obtaining a stably transfected packaging cell that made retroviral particles encoding SDI-1. Applicants discussion of "stably transfected" and "transiently transfected" is noted; however, applicants have not pointed to a reason why the teachings of Miller or Price are inadequate to obtain a "stably transduced" packaging cell as claimed.

Applicants argue it would not have been obvious to one of ordinary skill to make a packaging cell producing retroviral particles encoding SDI-1 because one of skill would have expected that SDI-1 expression would severely damage the cell due to inhibition of DNA synthesis. Applicants argument is not persuasive because Nabel taught packaging cells producing viral particles encoding SDI-1 produced viral particles (col. 6, line 22). Therefore, one of ordinary skill would have recognized that packaging cells producing retroviral particles encoding SDI-1 would not be severely damaged or be unable to produce viral particles because of SDI-1 expression. Furthermore, Nabel suggested making packaging cells producing retroviral particles (col. 3, line 10) and has a claim that encompasses treating restenosis using retroviral particles encoding SDI-1 (claim 1).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-2982.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL C. WILSON
PATENT EXAMINER